

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

H/B  
H. DAVIS  
04-20-98

Applicant: Ingham et al.

Serial No.: 08/\_\_\_\_,\_\_\_\_

Filed: 20 October 1997

Title: "Vertebrate Tissue Pattern-Inducing Proteins  
and Uses Related Thereto"

Attorney Docket

No.: HMV-006.11

Assistant Commissioner for Patents  
Washington, D.C. 20231

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I hereby certify that the instant Preliminary Amendment is being deposited with the United States Postal Services as express mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on the date set forth below.

10/20/97  
Date of Signature  
and Mail Deposit

By:

Matthew P. Vincent

Preliminary Amendment

Dear Sir:

Prior to examination, please amend the instant application as follows.

In the claims:

42. (new) A purified or recombinant polypeptide fragment of a *hedgehog* protein, which polypeptide modulates a hedgehog activity of the *hedgehog* protein.

43. (new) The polypeptide of claim 42, which polypeptide comprises an amino acid sequence designated in one of SEQ ID No:8, SEQ ID No:9, SEQ ID No:10, SEQ ID No:11, SEQ ID No:12, SEQ ID No:13 or SEQ ID No:14, or a sequence homologous thereto.

44. (new) A nucleic acid encoding a polypeptide fragment of a *hedgehog* protein, which polypeptide modulates a hedgehog activity of the *hedgehog* protein.

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45. (new) The nucleic acid of claim 21, which polypeptide comprises an amino acid sequence identical or homologous to an amino acid sequence designated in one of SEQ ID No:8, SEQ ID No:9, SEQ ID No:10, SEQ ID No:11, SEQ ID No:12, SEQ ID No:13 or SEQ ID No:14.

46. (new) A nucleic acid which encodes a polypeptide that modulates the biological activity of a *hedgehog* protein, which nucleic acid comprises a portion of the nucleotide sequence of the coding region of a gene identical or homologous to a sequence designated by one of SEQ ID No:1-7.

47. (new) A nucleic acid which encodes a polypeptide that modulates the biological activity of a *hedgehog* protein, which nucleic acid comprises a *hedgehog*-encoding portion that hybridizes under stringent conditions to a portion of the nucleotide sequence designated by one of SEQ ID No:1-7.

48. (new) An isolated and/or recombinantly produced *hedgehog* polypeptide comprising an amino acid sequence at least 80 percent identical with a *hedgehog* amino acid sequence selected from a group consisting of residues 27-425 of SEQ ID No:8, residues 22-396 of SEQ ID No:9, residues 1-336 of SEQ ID No:10, residues 25-437 of SEQ ID No:11, residues 24-418 of SEQ ID No:12, residues 24-475 of SEQ ID No:13, and residues 1-312 of SEQ ID No:14, or an extracellular fragment thereof of at least 150 contiguous amino acids, which polypeptide (i) binds to a *patched* protein, (ii) regulates differentiation of neuronal cells, (iii) regulates survival of differentiated neuronal cells, (iv) regulates proliferation of chondrocytes, (v) regulates proliferation of testicular germ line cells, or (vi) functionally replaces *drosophila hedgehog* in transgenic *drosophila* fly, or a combination thereof.

Respectfully submitted,

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